ANODIC OXIDATION OF 1,2,3,4-TETRAHYDRONAPHTHALENE AND ISOCHROMANE ANALOGUES OF 1-BENZYL AND 1-PHENETHYL ISOQUINOLINE ALKALOIDS. PRODUCTS AND MECHANISM OF THE INTRAMOLECULAR CYCLIZATION

by

Ulf Palmquist[a], Anders Nilsson[a], Vernon D. Parker[b], Tore Pettersson[a], and Alvin Ronlán[a,*]

Organic Chemistry 2, Chemical Center, University of Lund, P.O. Box 740, S-220 07 Lund 7, Sweden and Institute for Organic Chemistry, Norwegian Institute of Technology, 7034 Trondheim, Norway.

[a]University of Lund, [b] Norwegian Institute of Technology

*Author to whom correspondance should be addressed.

UNIV. LEIDEN BIBL.

ABSTRACT: The anodic oxidation of 1(3',4'-dimethoxybenzyl)-6,7-dimethoxy-(17a), 1(3',4'-dimethoxybenzyl)-1-methyl-6,7-dimethoxy- (17b), and 1(3',4'-dimethoxyphenethyl)-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene (17e), and 1(3',4'-dimethoxybenzyl)- (17c) and 1(3',4'-dimethoxybenzyl)-1-methyl-isochromane (17d) was studied by preparative electrolyses, cyclic voltammetry, and second harmonic a.c. measurements. With 17a-b, three different intramolecular coupling reactions were observed. The major reaction involved coupling between C-5a and C-14 leading, after demethylation, to a dienone of structure 18. The other cyclization reactions involved coupling between C-8a and C-14 with formation of an isomeric dienone (19) and coupling between C-4 and C-14 with formation of a 2,3,6,7-di(4',5'-dimethoxybenzo)-bicyclo(3,2,2)nonane derivative (21). For 17e the only reaction was coupling between C-8a and C-14 leading to the dienone 19c. With 17c-d there was intramolecular coupling between C-5a and C-14 giving the dienones 18c-d and between the heteroatom and C-14 giving, after hydrolysis, the hydroxylated compounds 24a-b. Second harmonic a.c. measurements indicated that all coupling reactions involved a very fast initial ECE reaction leading to a relatively stable cationic intermediate. The products observed can be rationalised readily in terms of known rearrangements and substitution reactions of these cations.

The intramolecular, oxidative coupling of phenols[1-3] and phenol ethers[4-15] of structures 1 or 2 has been studied in great detail (see Schemes 1 and 2). As can be seen, a wide variety of products are formed depending on solvent, oxidant and substitution pattern. In order to determine the importance of the heteroatom Z in structure 2 (Scheme 2) for the intramolecular coupling reaction and to find out whether or not ring B (structure 2) puts any steric restrictions on the cyclization reaction as compared to structure 1

Scheme 1

Scheme 2

Formula 17

1. M.A. Schwartz, B.F. Rose, R.A. Holton, S.W. Scott, and B. Vishnuvajjala, J. Am. Chem. Soc., 2571 (1977).
2. U. Palmquist, A. Nilsson, V.D. Parker, and A. Ronlán, J. Am. Chem. Soc., 98, 2571 (1976).
3. S.M. Kupchan, O.P. Dhingra, and C.-K. Kim, J. Org. Chem., 41, 4049 (1976).
4. A. Ronlán, O. Hammerich, and V.D. Parker, J. Am. Chem. Soc., 95, 7132 (1973).
5. V.D. Parker and A. Ronlán, Ibid., 97 4714 (1975).
6. A. Nilsson, U. Palmquist, A. Ronlán, and V.D. Parker, Ibid., 97, 3540 (1975).
7. A. Ronlán and V.D. Parker, J. Org. Chem., 39, 1014 (1974).
8. L.L. Miller, F.R. Stermitz, and J.R. Falck, J. Am. Chem. Soc., 95 2651 (1973).
9. J.R. Falck, L.L. Miller, and F.R. Stermitz, Ibid., 96, 2981 (1974).
10. L.L. Miller, F.R. Stermitz, J.Y. Becker, and V. Ramachandran, J., Ibid., 97, 2922 (1975).
11. S.M. Kupchan, V. Kameswaran, J.T. Lynn, D.K. Williams, and A.J. Liepa, Ibid., 97, 5622 (1975).
12. S.M. Kupchan and C.-K. Kim, Ibid., 97, 5623 (1975).
13. S.M. Kupchan, O.P Dhingra, C.-K. Kim, and V. Kameswaran, J. Org. Chem., 41, 4049 (1976).
14. A. Najafi and M. Sainsbury, Heterocycles, 6, 459 (1977).
15. I.W. Elliott, Jr., J. Org. Chem., 42, 1090 (1977).

---

we decided to investigate the carbon and oxygen analogues, 17a-e, of compounds 2a-d. The compounds 17b and 17e were included in this study in order to determine the reactivity of the benzylic position (C-1 in form-

ula 17).

RESULTS: The results of the preparative experiments are given in Table 1. The syntheses of the starting compounds 17a-e are outlined in Scheme 3. The identity of the electrolysis products 18-28 was established by spectroscopic methods. In the electrolysis of 17a three different dienones were isolated. Dienones obtained by coupling between positions 5 or 8 and 9 (formula 17) can be ruled out as none of the dienones isolated showed the required AB quartet (protons 13 and 14) in their n.m.r. spectra. Furthermore the protons of ring C always appear as two singlets in the spectra of the coupled products showing that ring C always couples at carbon 14 (formula 17). Only two different dienones can be formed by direct coupling, namely 18 (coupling between positions 5a and 14 in structure 17) and 19 (coupling between positions 8a and 14). However, it has been shown[11,15] that intermediates giving dienones of structure 19 (Z=NCHO or Z=O) undergo acid catalyzed rearrangement followed by demethylation to the dienones 20 and 20b. It therefore seems reasonable to assume that the three dienones obtained by electrolysis of 17a are 18a, 19a and 20a, an assumption which is supported by all spectroscopic data. Definite assignment of structure was achieved by analysis of the n.m.r. data, in particular the signals from the protons on carbons 9 and 13 (14) (structures 18-20). In compound 18a H-9 is allylic and the two H-13 are aliphatic, in 19a H-9 is aliphatic whereas the two H-13 are allylic, and in 20a both H-9 and the two H-13 are aliphatic (see Experimental for detailed assignments of n.m.r. peaks). The structures of the other dienones were established in a similar way by comparison of n.m.r. and i.r. data with those of compounds 18a-20a.

Formulas 18-28

Voltammetry results: Voltammetric data were obtained for the oxidation of compounds 17a, 17c, 17d and 17e and also for all the products from the

preparative scale electrolyses. The data in Table 2 were derived from results of cyclic voltammetry as well as fundamental and second harmonic a.c. measurements. A typical[§] cyclic voltammogram is that shown in Figure 1 from the oxidation of 17 d. The oxidation is an initial two-electron process which shows no indication of reversibility even at scan rates as high as 1,000 Vs^{-1} and a second quasi-reversible one-electron process at a potential about 300 mV more positive. The initial two-electron process is probably of the ECE[&] type since the second harmonic a.c. voltammograms were those expected for a reversible one-electron transfer, i.e. about 68 mV peak to peak separation[16].

---

16. A.M. Bond, R.J. O'Halloran, I. Ruzic and D.E. Smith, Anal. Chem., 48, 872 (1975).

The quasi-reversible redox couple O_2-R_2 (Fig. 1) also involves a one-electron transfer since the peak-to-peak separation in the second harmonic a.c. voltammogram was found to be close to 68 mV. The potentials for the quasi-reversible couples, O_2-R_2, for the reactive intermediates from oxidation of 17a-e where in all cases substantially greater than those of any of the products isolated from preparative electrolysis (see Table 2). The major products were the corresponding dienones (structures 18-20) which are oxidized at a potential approximately 100 mV more positive than for the substrates. The more positive potential associated with the oxidation of the reactive intermediates can thus be explained by assuming that they are positively charged. It is well known that cations derived from aromatic compounds are oxidized at more posi-

---

§ The same general pattern is observed for substrates 17a-c and 17e.

& E signifies a one-electron transfer process and C a chemical reaction such as deprotonation, demethylation, nucleophilic attack, etc.

tive potentials than the substrates, usually 300 mV or more†.

The voltammetric behaviour, and the product distribution from preparative electrolysis of compound 17a was found to be considerably more complicated than that from the other substrates. The voltammograms indicated that the initial two electron ECE process produces three different intermediates with reversible potentials more positive than the substrate (Table 2). None of the oxidation potentials of the products correspond to those observed during the voltammetric study of the oxidation of the substrate. It is thus quite likely that in this case there are three different ECE processes taking place and producing three different cationic intermediates which then react further to give the various products.

Coulometry: Coulometric oxidations[2] of 1 millimolar solutions of compounds 17b-e either in MeCN/$LiClO_4$ or MeCN/HBF_4 gave n-values close to 2. Compound 17a invariably gave coulometric n-values higher than 2.

DISCUSSION: The voltammetric data in Table 2 indicates that three different cationic intermediates are formed on anodic oxidation of compound 17a. In view of our product studies (Table 1) and earlier studies of related compounds[1-15] it appears resonable to ascribe the structures 34a, 35a, and 36a to these cationic intermediates. The observed reversible couples at 0.930, 1.050, and 1.185 V corresponds to a one-electron oxidation

---

† For example see ref. 17 for aromatic hydrocarbons and ref. 18 for methoxy-substituted aromatics.

17. O. Hammerich and V.D. Parker, J. Am. Chem. Soc., 96, 4289 (1974)

18. A. Ronlán, J. Coleman, O. Hammerich and V.D. Parker, J. Am. Chem. Soc., 96, 845 (1974)

of ring C to give a dication radical. The products observed can be rationalised in terms of the reactions shown in Scheme 4. The dienone 18a is formed via nucleophilic attack of water, when present*, followed by elimination of $MeOH_2^+$. In the same manner the dienone 19a is obtained from the cation 35a. The cation 35a can also rearrange in two different ways. One rearrangement (indicated with fully drawn arrows in structure 35) leads to dienone 20a (via nucleophilic attack of water and elimination of $MeOH_2^+$). The other (indicated with a dotted arrow) leads to the aromatic structure 23a after loss of a proton. The latter product is observed only in solvents of low nucleophilicity and in the presence of acid (Exp. 6 in Table 1), in accordance with our previous observations[4-7] of similar rearrangements during anodic cyclisation of compounds with structure 1. The highest yield of the dienone 19a was obtained in neutral solution (Experiments 1 and 4 in Table 1). In the presence of HBF_4/H_2O 19a was not observed (Exp. 2) and in the presence of H_2SO_4/H_2O the yield of 19a was more than halved (Exp. 3). This decrease in the yield of 19a is not accompanied by any considerable increase in the yield of any of the other products. This indicates that the acid catalyses the rearrangement of 35a to 23a at the expense of rearrangement leading to 20a (the yield of this product is fairly constant). 23a is more easily oxidised than the substrate and is converted to its cation radical which is stable only in TFA/DCM. In the other electrolytes the cation radical probably undergoes nucleophilic substitution followed by further oxidation with formation of intractable tars.§ A decrease of the electrolysis temperature from -35°C (Exp. 1) to -81°C (Exp. 4) resulted in a

---

* In acetonitrile there are usually trace amounts of water present. However, it is also possible that acetonitrile itself functions in a similar manner as a nucleophile and in this case will give a nitrilium ion which undergoes hydrolysis to 18a during work-up.

§ It is possible that the dienone 19a undergoes acid catalysed rearrangement to a phenol of similar structure as 23a (OH group on C-7) which is destroyed by further oxidation.

drastic increase of the yield of 21a and an improvement in the current yield. This probably depends on a lower H_2O conc. and activity in EtCN at -81°C and an increased stability of the cation radical formed by oxidation of 21a (this compound is more easily oxidised than 17a) or of the cation 36a. In general the improvements in yield at lower temperatures are in part dependent on the increased stability of the products. The results from Exp. 1 and 4 do not indicate any effect of the temperature on the relative rates of the cyclization reactions leading to 18a, 19a, and 20a. In contrast the addition of H_3O^+ (as 35% aqueous HBF_4) seems to affect the relative rates of the cyclization reactions. Comparison of experiments 1 and 2, 9 and 10-12, and 15 and 16 clearly shows that the rate of the cyclization reaction leading to dienones of structure 18 increases more than the other cyclization reactions in going from acetonitrile/$LiBF_4$ to the acetonitrile/HBF_4 as electrolyte. In Scheme 4 we have suggested that the cyclization product 21 is formed via rearrangement of the cation 36 which is formed by coupling between the benzylic C-4 carbon and C-9 in ring C (structure 17).† Structure 21 could also arise by rearrangement of the cation 34 (bond shift from C-5a to C-13): However, in that case only two cationic intermediates should be observed in the second harmonic a.c. measurements (Table 2). Furthermore the oxidation of 17a in methanol (Exp. 5, Table 1) shows that the bensyl cation 37 is formed during anodic oxidation of 17a-b.

---

† Direct coupling between C-4 and C-14 in 37 followed by deprotonation also gives 21. However, in all our previous studies of similar couplings[4-7] the initial electrophilic attack has always occurred in the substituted ortho position with formation of a charged intermediate which rearranges to give the final product

The results of the anodic oxidations of compounds 17c-d can be rationalised in terms of the mechanisms in Scheme 4 in a similar way as for 17a. It is interesting that the yield of the dienone 18b is much better than that of 18a in the presence of HBF_4 (Exp. 2 and 9 in Table 1) and that coupling in the phenethyl analogue 17d only occurs between C-8a and C-10 (structure 17).

No dienones (18c-d) are formed on electrolysis of compounds 17c-d in the absence of water (Exp. 16 and 17). only the hydroxylated compound 24, the tetralone 26, veratric aldehyde (27), and the oxidation product (28) of veratric aldehyde are observed. Two possible mechanisms for the formation of these products are outlined in Scheme 5. In the first the radical cation $17^{+\cdot}$ is formed by selective oxidation of ring C. Nucleophilic attack of the oxygen in ring B on the cation radical moiety followed by further oxidation and deprotonation gives the cation 38 which on hydrolysis yields 24. Deprotonation of $17^{+\cdot}$ followed by further oxidation yields a benzylic cation which undergoes intramolecular nucleophilic attack to give the cation 39 which is then hydrolysed to the glycol 40. Further oxidation of 40 results in the usual glycol cleavage to form veratric aldehyde (27) and 26. In the second mechanism, 24 is formed via the cation 34 by intramolecular nucleophilic substitution as in Scheme 5. However, it is difficult to explain the formation of 26 and 27 from 34. Possibly both mechanisms are operative and in the absence of external nucleophiles 34 only undergoes intramolecular nucleophilic substitution to give 38. If an external nucleophile such as water is added the reaction leading to 18 becomes fast enough to compete with the reaction leading to 24 (Scheme 5). However, the present data does not allow any definite assignment of mechanisms.

Synthetic applications: It should be noted firstly that the coupling to ring C always occurs at C-14, no coupling at C-10 was observed*. In contrast coupling in ring A occurs directly at both C-5a and C-8a and indirectly at C-8 (Formula 17) giving structures 18-20 and 23. The yields of the dienones 18-19 and of the compound 23 are good and our experiments indicate that it should be possible to achieve fairly selective formation of either 18 or 19 (20 is always a minor product) or 23 by simple changes in the electrolysis conditions (pH, addition of TFA, etc.). Of more special interest is the possibility of introducing a hydroxy group in the C-14 position of benzyl- or phenethyl- isochromanes similar to 17c-d via the indirect oxidation in Scheme 5.

Conclusions: Ring B in structure 17 does not appear to put any steric restraints on the coupling between rings A and C since the same types of product and similar yields are obtained in the anodic coupling of compounds of structure 1. The hetero atom Z in 2 and 17 appears to be without effect on the coupling between rings A and C. However, due to the nucleophilicity of oxygen and nitrogen[14] a competing intramolecular cyclization reaction can occur. This involves nucleophilic attack of Z (=O or N) on ring C after oxidation to the cation radical or the cation at the anode (see Scheme 5). It is of interest to note that this intramolecular nucleophilic reaction can be inhibited completely by addition of strong acid when Z=N (protonation of nitrogen; see 2→8 in Scheme 2). The C-1 methyl group in structure 17 does not affect the product pattern or voltammetry compared with that of the compounds without a C-1 methyl, indicating that the reactivity of the C-1 position is low compared to that of the C-4 position.

EXPERIMENTAL:

General procedures and apparatus used for voltammetry and coulometry and for the purification of solvents were conventional and have been described previously[2]. The NMR spectra were recorded in deuteriochloroform with Me_4Si as internal reference. Ir spectra were recorded using KBr tablets (solids) or thin films (liquids). High resolution mass spectra were recorded with a Varian MAT 311 instrument.

Synthesis of 1(3',4'-dimethoxybenzyl)-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene (17a).

1,5-Bis(3,4-dimethoxyphenyl)-3-pentanone (41). 3,3', 4,4'-Tetramethoxybenzalacetone (29)[19], mp 124-125°C, 70.8 g, 0.2 mol, was dissolved in ethanol, 300 ml, and submitted to catalytic hydrogenation at 1 atm. with Pd/C (10%), 5g, as catalyst. When the theoretical amount of hydrogen had been consumed, the catalyst was filtered off and the filtrate evaporated to yield pure 41, 80.2 (100%), Mp 83-84°C; NMR δ 6.77(6H, m, ArH), 3.90(12H, s, OCH_3), 2.80(8H, m, CH_2) ppm.

19. Org. Synthesis Coll. Vol. I, 105 (1941).

1,5-Bis(3,4-dimethoxyphenyl)-3-pentanol (42). 41, 46.3 g (0.129 mol), was dispersed in methanol, 150 ml, KBH_4, 3.5 g (0.065 mol), dissolved in a 1:3 mixture of 0.1 M aqueous NaOH and methanol was added with stirring during 0.5 h. Stirring was continued at room temperature for 4 h and then water, 250 ml, was added to precipitate 42. Yield 45.3 g (97%), Mp 89-91°C. NMR δ 6.75(6H, s, ArH), 3.83(12H, s, OCH_3), 2.75(5H, m, $ArCH_2$, CHOH), 1.70(4H, m, CH_2) ppm.

17a. 42, 9.90 g(27.5 mmol), dissolved in dry nitromethane, 100 ml, was heated to 90°C and $SnCl_4$, 14.30 g(55mmol), was added dropwise with stirring. The reaction mixture was kept at 90°C (dry atmosphere) for 2 h and then poured on a mixture of ice, 200 g, and conc. HCl, 50 ml. This mixture was

stirred until no further colour changes occurred and then extracted with ether, 2x100 ml, The combined ether extracts were washed with satd. bicarbonate solution and water, dried over sodium sulfate, and evaporated to yield a yellow oil, 8.00 g which was purified by filtration through alumina (methylene chloride eluent). Yield 7.50 g(80%) of a colourless oil which crystallized after standing several months. The oil was identified as from spectroscopic data for a crystalline sample obtained by chromatography on silica gel (di-iso-propyl ether eluent): Mp 80-81°C; NMR, δ 6.83(3H, m, C-ArH*), 6.50(1H, s, A-ArH), 6.45(1H, s, A-ArH, 3.80(9H, s, OCH_3), 3.70(3H, s, OCH_3), 2.73(5H, m, $ArCH_2$, ArCH), 1.70(4H, m, B-CH_2) ppm.

Anal. Calcd. for $C_{21}H_{26}O_4$: 342.1766. Found: 342.1798.

Synthesis of 1(3',4'-dimethoxybenzyl)-1-methyl-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene (17b)

1.5-Bis(3,4-dimethoxyphenyl)-2-methyl-2-pentanol (30): 1-Bromo-3-(3,4-dimethoxyphenyl)-propane, 5.18 g (20 mmol), dissolved in dry tetrahydrofuran (THF), 25 ml, was added slowly to magnesium filings, (5 g preactivated with 5-10 drops of 1,2-dibromoethane) covered with THF in a carefully dried three-neck flask (nitrogen atmosphere). The reaction mixture was refluxed for half an hour and after cooling 1(3,3-dimethoxyphenyl)-2-propanone, 3.88 g(20 mmol), dissolved in dry THF, 15 ml, was added slowly. After refluxing for 2 h under N_2 the mixture was allowed to cool and poured on ice, 150 g, neutralised with dil HCl, and extracted with ether, 2x75 ml. The combined ether extracts were washed with water, dried over sodium sulphate, and evaporated to yield a yellowish oil, 6.10 g, which according to its NMR spectrum was a mixture of 30, and the propane and propanone starting materials. The two latter compounds were removed by

*C-ArH indicates the protons on ring C in structures 17-21; A-ArH indicates the protons on ring A in structures 17-21, etc.

distillation at 0.1 mm. The residue, 4.91 g was identified as 30 by its NMR: δ 6.72(6H, s, ArH), 3.87(12H, s, OCH_3), 2.70(2H, s, $ArCH_2$), 2.60(2H, m, $ArCH_2$), 1.62(4H, m, CH_2), 1.17(3H, s, CH_3) ppm. Yield 65%.

17b: 30, 3.74 g (10 mmol) was dissolved in dry methylene chloride, 100 ml contained in a flask fitted with a magnetic stirring bar and a drying tube. With stirring trifluoromethane sulfonic acid (TFMS), 3.00 g (20 mmol) was added dropwise. After stirring for 2 h at room temperature the solution was extracted with water, 50 ml, satd. $NaHCO_3$, 50 ml, and water, 50 ml, dried over sodium sulfate,and evaporated to give a a yellow oil, 3.30 g which was purified by filtration through alumina (20 g, methylene chloride eluent). Yield 3.06 g(86%) of a colourless oil identified as 17b from the spectroscopic data below,obtained from a crystalline sample made by rechromatography of the oil on silica gel (di-iso-propyl ether eluent) followed by recrystallization from ethanol. Mp 90-91°C, NMR δ 6.63(5H,m,ArH), 3.93 (6H,s,OCH_3), 3.87(3H,s,OCH_3), 3.75(3H,s,OCH_3), 2.87(2H,m,C-$ArCH_2$), 2.63(2H,m,A-$ArCH_2$) 1.70(4H,m,CH_2), 1.33(3H,s,CH_3) ppm.

Anal. Calcd for $C_{22}H_{28}O_4$: 356.1987. Found: 356.1975.

Synthesis of 1(3',4'-dimethoxybenzyl)-6,7-dimethoxyisochromane (17c):

Alternative A:

2-Carboxymethyl-4,5,3',4'-tetramethoxy-deoxybenzoin (32): 3,4-Dimethoxyphenyl acetic acid, 19.6 g (0.1 mol), and polyphosphoric acid (PPA), 150 g, were thoroughly mixed and heated to 80°C for 30 min[20]. Then the mixture was slowly poured on ice

---

20. D.C. Ayres and R.C. Denney, J. Chem. Soc., 1961, 4506.

---

and stirred until the red colour had disappeared (this sometimes required gentle warming), and extracted with methylene chloride, 3x150 ml. The combined extracts were washed with water, 2x100 ml, dried over sodium sulfate, and evaporated to give a yellow oil, 16.72 g,which after crystallization from ethanol afforded 32, 13.71 (73%). Mp 153-155°C. NMR δ 7.37(1H,s,ArH_6), 6.80(4H,s,ArH), 4.20(4H,s,$ArCH_2CO$),

3.90(3H,s,OCH_3), 3.85(3H,s,OCH_3), 3.82(3H,s,OCH_3), 3.78(3H,s,OCH_3) ppm.

17c: 32, 13.22 g (35.3 mmol), was added in small portions to a stirred mixture of $LiAlH_4$, 4.50 g (132 mmol), in dry THF, 250 ml, kept under nitrogen. After the addition stirring was continued for 2 h more at room temperature. The reaction mixture was then cooled and water, 100 ml, was added slowly followed by 2M HCl to acidic reaction. A further 300 ml ml of water was added and the mixture was extracted with ether, 6x100 ml. The combined ether extracts were washed with water, 100 ml, dried over sodium sulfate, and evaporated to give a viscous, colourless oil, 12.17 g, which NMR indicated to contain 50% of 17c. This oil was dissolved in chloroform, 100 ml, contained in a roundbottomed flask fitted with a magnetic stirring bar and a Soxhlet extractor containing molecular sieves, 3A 4g. p-Toluene sulfonic acid, 250 mg (1.54 mmol), was added and the mixture was reflux for one h, cooled, extracted with satd. $NaHCO_3$, 75 ml, water, 75 ml, dried over sodium sulfate, and evaporated to give an oil 11.57 g, which crystallized upon sta ding over night. Recrystallization from ethanol gave 17c, 9.97 g (82%), identified by its Mp 91-92°C; NMR δ 6.80 (3H,s,C-ArH), 6.60(1H,s,A-ArH_5), 6.53(1H,s,A-ArH_8), 4.93(1H,t(J=6Hz),ArCH), 3.93(2H,q(J=5Hz),OCH_2), 3.88(9H,s,OCH_3) 3.80(3H,s,OCH_3), 3.08(2H,d(J=6Hz), C-$ArCH_2$), 2.72(2H,q,J=5Hz,A-$ArCH_2$) ppm.

Anal. Calcd for $C_{20}H_{24}O_5$: 344.1623. Found: 344.1602.

Alternative B:

17c: A mixture[21] of homoveratroylalcohol, 1.82 g (10 mmol), dicyclohexyl carbodiimi (DCC), 6.30 g (30 mmol), dimethyl sulphoxide (DMSO), 15 ml, TFA, 0.4 ml (10 mmol) pyridine, 0.8 ml (10 mmol), and dry methylene chloride, 35 ml, was stirred for 24

---

21. K.E. Pfitzner and J.G. Moffat, J. Am. Chem. Soc., 87, 5661, 5670 (1965).

---

and then poured into ether, 200 ml, and oxalic acid, 2.70 g (30 mmol), was added in small portions. The precipitated crystals were filtered off and the filtrate was washed with satd. $NaHCO_3$, 50 ml, and water, 2x75 ml, dried over sodium sulfate an

evaporated to give a yellow oil, 1.88 g, which according to its NMR contained homoveratrumaldehyde, 66%, and homoveratrylalcohol, 30%. This oil was dissolved in methylene chloride, 100 ml, contained in a roundbottomed flask fitted with a magnetic stirring bar and a Soxhlet extractor containing molecular sieves, 3A 3g. Homoveratrylalcohol, 0.65 g (3.6 mmol) and p-toluene sulfonic acid, 0.1 (0.6 mmol), was added and the mixture was refluxed for 2 h, cooled, extracted with satd. $NaHCO_3$, 75 ml, and water, 75 ml, and evaporated to give a yellow oil, 2.51 g, which on crystal ization from ethanol yielded 17c, 1.76 g (75%), identical with the product obtained by alt. A.

Synthesis of 1(3',4'-dimethoxybenzyl)-1-methyl-6,7-dimethoxyisochromane (17d): Homoveratrylalcohol, 9.10 g (50 mmol), 3,4-dimethoxyphenyl-2-propanone, 9.80 g (50 mmol), and p-toluene sulfonic acid, 1.00 g (6.1 mmol), was dissolved in chloroform, 150 ml, contained in a roundbottomed flask fitted with a magnetic stirring bar and a Soxhlet extractor and refluxed for 20 h. After cooling the reaction mixture was extracted with satd. $NaHCO_3$, 100 ml, water, 100 ml, dried and evaporated to give a yellow oil, 17.83 g, which crystallized upon standing. Recrystallization from methanol afforded 17d, 16.68 g (93%), identified by its Mp 80-81°C; NMR δ 6.63(5H,m, ArH), 3.90(2H,t,OCH_2), 3.88(9H,s,OCH_3), 3.77(3H,s,OCH_3), 3.03(2H,d, C-$ArCH_2$), 2.55(2H,t(J=6Hz),A-$ArCH_2$).

Anal. Calcd for $C_{21}H_{26}O_5$: 358.1779. Found: 358.1786.

Synthesis of 1(3',4'-dimethoxyphenethyl)-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene (17e)

1,6-Bis(3,4dimethoxyphenyl)-hex-3-en-1,6-dion (33): Trans-β-hydromuconic acid, 43.2 g (0.3 mol) and freshly destilled $SOCl_2$ was refluxed together for 2 h. Excess $SOCl_2$ was detstilled off and the residue was dissolved in dry chloroform, 150 ml, and slowly mixed with $AlCl_3$, 120 g (0.9 mol), and dry chloroform, 400 ml. With mechanical stirring veratrol, 91 ml (0.6 mol) was added dropwise. The resulting slurry was stirred for 18 h with reflux and then poured on a mixture of ice, 1000 g, and conc. HCl, 200 ml. The organic phase was separated and the aqueous phase was extracted several times with chloroform. The combined organic phases were washed

with satd. $NaHCO_3$ and water, dried over sodium sulfate, and evaporated to give a semicrystalline mass, 65 g. Recrystallisation from methanol yielded 33, 52.4 g (52%), Mp 159-160°C; NMR δ 7.50(2H,d(J=8Hz),ArH), 7.42(2H,s,ArH), 6.78(2H,d(J=8 ArH), 5.80(2H,m,olephinic-H), 3.87(12H,s,OCH_3), 3.68(4H,m,CH_2) ppm.

1,6-Bis(3,4-dimethoxyphenyl)-3-hexene (43): 33, 76.8 g (0.22 mol), zink amalgame from Hg_2Cl_2, 17.1 g, and zink, 171 g, as described in ref.22, conc. HCl, 140 ml, water, 105 ml, and toluene, 140 ml, were refluxed together with vigorous stirrir

---

22. L.F. Fieser and M. Fieser, Reagent for Organic Synthesis, Vol.I, 1287, Wiley N.Y. 1967.

---

for 24 h. Every sixth hour conc. HCl, 70 ml, was added. After cooling the organic phase was separated and the aqeous phase was extracted with ether, 2x250 ml. The combined organic phases were washed with water, 250 ml, dried over sodium sulfate and evaporated to give a colourless oil, 57.3 g which on crystallization from methanol yilded the hexene, 52.0 g (73%), Mp 80-82°C; NMR δ 6.73(6H,m,ArH), 5.50(2H m,olephinic-H), 3.87(12H,s,OCH_3), 2.50(8H,m,CH_2) ppm.

17e: 43, 2.50 g (7.0 mmol) and TFMSA, 0.25 g (1.7 mmol), was dissolved in dry methylene chloride, 100 ml, stirred for 2 h at room temperature (dry atmosphere), and then washed with stad. $NaHCO_3$, 50 ml, and water, 50 ml, dried over sodium sulfate, and evaporated to give 17e as a yellowish oil, 2.50 g (100%), which crystallized slowly on standing. This product was used in the electrolyses experiments. An analytical sample of 17e was obtained by chromatography on alumina (activity 2-3 according to Brockman, ether:methylene chloride = 1:1 as eluent) followed by recrystallisation from ethanol. Mp 59-61°C; NMR δ 6.67(5H,m,ArH), 3.85(12H,s,OCH_3) 2.70(5H,m,ArCH,$ArCH_2$), 1.83(6H,m,CH_2) ppm.

Anal. Calcd for $C_{22}H_{28}O_4$: 359.1986. Found: 359.1961.

Electrolysis. General: The electrolyses were conducted in a closed one-compartment cell fitted with a cooling mantel and a magnetic stirring bar. The anode was a platinum cylinder (50 cm^2), the cathode a coiled nickel wire (diam. 1.25 mm,

lenght 40 cm), and the reference electrode was either a saturated calomel electrode a Ag/Ag^+ electrode. The compound to be electrolyzed, 1.5 mmol, was dissolved in the elctrolyte[§], 60 ml, and submitted to constant potential electrolysis. After the elctrolysis the elctrolyte was poured into water (or satd. $NaHCO_3$ when the electrolyte contained acid), 300 ml. The organic phase was separated and the aqueous phase was extracted with methylene chloride, 2x100 ml,. The combined organic phases were washed with water, dried over sodium sulfate, and evaporated. The residue was filtered through alumina (activity 2-3, methylene chloride eluent) when dienones were to be isolated and through silica gel (methylene chloride eluent) when phenols were to be isolated. The product obtained after evaporation of the methylene chloride was analyzed as described below.

[§] Commercial, p.a. quality solvents stored over molecular sieves were used.

Analysis of electrolysis products. Isolation procedure.

The cyclized products (ortho-para coupling), 22 and 23b, from electrolysis of 17a and 17b were isolated by chromatography on silica gel with diisopropyl ether as eluant. The other oxidation products from 17a and 17b were isolated by rechromatography on alumina (activity 2-3) with ether:methylene chloride = 1:1 as eluent. The products were eluted in the following order: 21a, 17a, 20a, and (18a + 19a). The products from 17b appeared in a similar way. 18a and 19a were separated by chromatography on a celite/activated carbon column (1:1, methylene chloride eluent). Once 19a had been obtained in crystalline form it become possible to crystallize the compound from the crude electrolysis product dissolved in ethanol by seeding (the same was the case with 18b).

Compound 25 was isolated by chromatography on alumina with ether as eluent. Compound 23c was isolated by direct crystallization of the residue (vide supra) from ethanol.

The isolation of the products from oxidation of 17c and 17d was quite troublesome. The hydroxylated products 24a-b do not survive chromatography on alumina and the dienones 18c-d,and to some extent also 24a-b, decompose on silica gel. We found it necessary to run separate experiments in order to isolate all products.

In the first the elctrolysis product was chromatographed on alumina (ether:methylene chloride = 1:1 as eluent) and the dienones 18c and 18d were isolated while the hydroxylated products were lost. In the second the dienone was precipitated from the electrolysis product dissolved in ethanol by seeding with pure, crystalli dienone from the first experiment. After evaporation of the ethanol the residue was chromatographed on silica gel at -15°C with ether:methylene chloride (1:1) as eluent and 23a and 23b were obtained in a pure state.

Product 22 from 17a: Mp 99-100°C. NMR δ 9.27(1H,s,ArH), 7.30(1H,s,ArH), 7.13 (1H,s,ArH), 7.07(1H,s,ArH), 4.05(3H,s.OCH_3), 4.02(6H,s,OCH_3), 3.93(3H,s,OCH_3), 3.12(4H,m,$ArCH_2$), 2.07(2H,m,CH_2) ppm. IR ν 2940, 2840, 1620, 1600, 1520, 1470 cm^{-1}

Anal. Calcd for $C_{21}H_{22}O_4$: 338.1517. Found: 338.1496.

Dienone 18a from 17a: Mp 99-101 and 138-139°C. NMR δ 6.87(1H_8,s), 6.65(1H_4,s), 6.40(1H_1,s), 6.30(1H_5,s), 3.92(3H,s.OCH_3), 3.88(3H,s,OCH_3), 3.81(3H,s,OCH_3), 3.10(3H,m,H_9 and H_{10}), 2.00 (2H,m,H_{13}), 1.57(4H,m,H_{11}-H_{12}) ppm. IR υ 2940, 2850, 16665, 1640, 1620, 1520, 1470 cm^{-1}.

Anal. Calcd for $C_{20}H_{22}O_4$: 326.1518. Found: 326.1521.

Dienone 19a from 17a: Mp 168-171°C. NMR δ 6.98(1H_8,s), 6.68(1H_4,s), 6.45(1H_1,s), 5.98(1H_5,s), 3.93(6H,s,OCH_3), 3.73(3H,s,OCH_3), 2.67(4H,m,$H_{10}$and H_{13}), 1.73(5H,m, H_9,$H_{11}$and H_{12}) ppm. IR ν 3090, 2985, 2840, 1665, 1640, 1595, 1520, 1460 cm^{-1}.

Anal. Calcd for $C_{20}H_{22}O_4$: 326.1517. Found 326.1478.

Dienone 20a from 17a: Mp 166-167°C. NMR δ 6.86(1H_5,s), 6.42(1H_4,s), 6.27(1H_1,s), 5.80(1H_8,s), 3.92(3H,s,OCH_3), 3.78(3H,s,OCH_3), 3.60(3H,s,OCH_3), 2.48(3H,m,$H_9$and H 1.78(2H,m,H_{13}), 1.20(4H,m, $H_{11}$and H_{12}) ppm.

Anal. Calcd for $C_{20}H_{22}O_4$: 326.1518. Found: 326.1534.

Product 21a from 17a: Mp 161-163°C. NMR δ 6.82(1H,s,ArH), 6.77(1H,s.ArH), 6.73(1H s,ArH), 6.53(1H,s,ArH), 3.90(9H,s,OCH_3), 3.80(3H,s,OCH_3), 3.75(1H_5,m), 3.16(1H_{10},m 2.10(4H,m,H_{12-13}) ppm. IR ύ 3000, 2940, 2840, 1615,1520, 1470 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_4$: 340.1674. Found: 346.1675.

Tetralone 25 from 17a: Mp 127-128.5°C. NMR δ7.55(1H,s,ArH), 6.70(3H,m,ArH), 6.40(1H, s,ArH), 3.92(3H,s,OCH_3), 3.88(3H,s,OCH_3), 3.86(3H,s,OCH_3), 3.77(3H,s,OCH_3), 2.87(5H, m,H_1,H_3 and $ArCH_2$), 2.13(2H,m,H_2) ppm. IR ν 2930, 2840, 1670, 1600,1510 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_5$: 356.1623. Found: 356.1596.

Dienone 18b from 17b: Mp 169-170°C. NMR δ 6.80(1H_8,s), 6.57(1H_4,s), 6.40(1H_1,s), 6.30(1H_5,s), 3.88(3H,s,OCH_3), 3.83(3H,s,OCH_3), 3.80(3H,s,OCH_3), 2.93(2H,s,H_{10}), 1.95(2H,m,H_{13}), 1.48(4H,m,H_{11-12}), 1.28(3H,s,CH_3) ppm. IR ν 3000, 2940, 2840, 1670, 1640, 1620, 1520, 1465 cm^{-1}. C^{13}NMR δ 181.16(s), 169.63(s), 150.80(s), 148.04(2s, overlapping), 130.51(s), 129.38(s), 120.45(2s, overlapping), 110.06(d), 108.27(d), 56.33(q), 55.84(q), 54.87(q), 46.26(t), 45.13(s), 44.48(t), 43.34(t), 37.98(s), 27.43(q), 19.64(t) ppm.

Anal. Calcd for $C_{21}H_{24}O_4$:340.1674. Found: 340.1655.

Dienone 19b from 17b: Mp 81-83°C and 142-145°C. NMR 7.10(1H_8,s), 6.73(1H_4,s), 6.57(1H_1,s), 6.00(1H_5,s), 3.90(6H,s,OCH_3), 3.73(3H,s,OCH_3),2.81(2H,q(J=16Hz),H_{10}), 2.00(6H,m,H_{11-13}), 0.98(3H,s,CH_3) ppm. C^{13}NMR δ 181.48(s),158.92(s), 151.43(s), 151.13(s), 148.04(s), 129.54(s), 123.53(d), 123.37(s), 118.50(d), 110.87(d), 107.30(d), 56.00(q,two overlaapping), 55.03(q), 53.89(s), 49.83(s), 40.23(t), 39.28(t, two overlapping), 22.56(q), 21.59(t) ppm. IR ν 3000, 2960, 2840, 1660, 1640, 1595, 1520, 1670 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_4$: 340.1674. Found: 340.1636.

Dienone 20b from 17b: Mp 112-114°C. NMR δ 6.82(1H_5,s), 6.38(1H_4,s), 6.22(1H_1,s), 5.68(1H_8,s), 3.87(3H,s,OCH_3), 3.73(3H,s,OCH_3), 3.55(3H,s,OCH_3), 2.88(2H,q(J=16Hz), H_{10}), 2.27(2H,m,H_{13}), 1.60(4H,m,H_{11-12}), 1.10(3H,s,CH_3) ppm.IR ν 3000, 2940, 2860, 1670, 1640, 1620, 1505, 1470 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_4$: 340.1674. Found: 340.1671.

Product 23b from 17b: Mp 103-105°C. NMR δ 8.02(1H,s,ArH), 6.70(1H,s,ArH), 6.56(1H, s,ArH), 3.93(3H,s,OCH_3), 3.88(3H,s,OCH_3), 3.65(3H,s,OCH_3), 2.78(4H,m,$ArCH_2$), 1.73 (4H,m,CH_2), 0.88(3H,s,CH_3) ppm. IR ν 2920, 2840, 1610, 1600, 1575, 1510, 1470 cm^{-1}.

Anal. Calcd for $C_{22}H_{26}O_4$: 354.1825. Found: 354.1828.

Dienenone 18c from 17c: 184-186°C. NMR δ 6.85(1H_8,s), 6.67(1H_4,s), 6.42(1H_1,s), 6.32(1H_5,s), 4.38(1H_9,t(J=4Hz)), 3.85(3H,s,OCH_3),3.82(3H,s,OCH_3), 3.77(3H,s,OCH_3) 3.73(2H_{12},m) , 3.33(2H_{10},d(J=4Hz)), 1.98(2H_{13},m) ppm. IR ν 3010, 2980, 2960, 2920, 2875, 1680, 1660, 1640, 1630, 1520, 1470 cm^{-1}.

Anal. Calcd for $C_{20}H_{24}O_5$:328.1311. Found: 328.1324.

1(3',4'dimethoxy-6'-hydroxybenzyl)-6,7-dimethoxyisochromane (23a): Obtained as an oil which NMR and TLC indicated to be a single compound. NMR δ 6.88(1H,s,C-ArH_2), 6.77(2H,s,ArH), 6.63(1H,s,ArH), 3.93(3H,s,OCH_3) 3.90(1H_1,m), 3.85(3H,s,OCH_3), 3.82(3H,s,OCH_3), 3.68(2H_3,t(J=6.5Hz)), 3.47(2H,d(J=2.5Hz),C-$ArCH_2$), 2.62(2H_4,t(J=2.5Hz)) ppm. IR ν 3000, 2940, 2840, 1610, 1510,1470 cm^{-1}. Mass 360 (M^+) m/e.

If 23a was dissolved in CD_3OD/D_2O (1:1) and left for 1 h the mass of the molecular ion of the residue obtained on evaporation of the solvent changed to 361.

Product 28 from 17c: Mp 251-253°C. NMR δ 7.03(2H,s,ArH), 6.93(2H,s,ArH), 4.30(4H,sAA,$ArCH_2$), 4.00(6H,s,OCH_3), 3.97(6H,s,OCH_3) ppm.

Anal. Calcd for $C_{18}H_{20}O_5$: 316.1311. Found: 316.1299.

Compound 26 from 17c or 17d: Mp 138-140°C. NMR δ 7.53(1H,s,ArH), 6.70(1H,s,ArH), 4.53(2H,t(J=6Hz),OCH_2), 3.97(3H,s,OCH_3), 3.95(3H,s,OCH_3), 3.00(2H,t(J=6Hz),$ArCH_2$) ppm. Mass 208(M^+) m/e.

Dienone 18d from 17d: Mp 162-164°C. NMR δ 6.90(1H_8,s), 6.65(1H_4,s), 6.47(1H_1,s), 6.38(1H_5,s), 3.93(3H,s,OCH_3), 3.88(3H,s,OCH_3), 3.85(3H,s,OCH_3), 3.77(2H_{12},t(J=5.5H 3.25(2H_{10},s(broad)), 1.95(2H_{13},t(J=5.5Hz)), 1.55(3H,s(broad),CH_3) ppm. IR ν 3000, 2950, 2880,2850, 1675,1650, 1625, 1525, 1460 cm^{-1}.

Anal. Calcd for $C_{20}H_{22}O_5$: 342.1466. Found: 342.1460.

1(3',4'-dimethxoy-6'-hydroxybenzyl)-1-methyl-6,7dimethoxyisochromane (24b): Mp 57-59°C NMR δ 6.85(1H,s,ArH_2), 6.73(2H,s,ArH), 6.63(1H,s,ArH), 3.95(3H,s,OCH_3), 3.92(3H, s,OCH_3), 3.87(3H,s,OCH_3), 3.83(3H,s,OCH_3), 3.67(2H_3,t(J=7Hz)), 3.47(2H,s,C-$ArCH_2$) 2.58(2H_4, t(J=7Hz)), 1.98(3H,s,CH_3) ppm.

Anal. Calcd for $C_{21}H_{26}O_6$: 374.1729. Found: 374.1757.

Product 23c from 17e: 131-133°C. NMR δ 7.13(1H,s,ArH), 6.77(1H,s,ArH),6.67(1H,s,ArH) 3.93(3H,s,OCH_3), 3.88(6H,s,OCH_3), 3.45(3H,s,OCH_3), 2.80-1.70(11H,m) ppm. IR ν 3000, 2930, 2860, 1610, 1600, 1580, 1520, 1470 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_4$:354.1831. Found: 354,1806.

Dienone 19c from 17e: Mp 134-136°C. NMR δ 6.63($1H_8$,s), 6.42($1H_4$,s), 6.22($1H_1$,s), 6.13($1H_5$,s), 3.88(3H,s,OCH_3), 3.68(3H,s,OCH_3), 3.60(3H,s,OCH_3), 3.10-1.40(11H,m) ppm. IR ν 3000, 2940, 2860, 1670, 1640, 1615, 1515, 1470 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_4$: 340.1674. Found: 340.1699.

Acknowledgement. This research was supported by a grant from the Swedish Natural science Research Council.

Preparative anodic oxidations of compounds 17a-e[1].

Entry	Compound	Electrolyte	Temp	E(V)[2]	C(%)[3]	Products, yield(%)[4]
1	17a	MeCN, $LiBF_4$[5]	-35°C	0.85	93	18a(33); 19a(29); 20a(6); 21a(>0)
2	17a	MeCN, HBF_4[6]	-35	0.85	100	18a(48); 20a(6); 21a(>0)
3	17a	MeCN, H_2SO_4, H_2O[7]	-35	0.85	95	18a(30); 19a(11); 20a(3); 21a(>0)
4	17a	EtCN, $LiBF_4$[5]	-81	0.85	100	18a(41); 19a(21); 20a(2); 21a(13)
5	17a	MeOH, K_2CO_3	+10	1.2	30	25(62)
6	17a	DCM-TFA, Bu_4NBF_4[8]	0	0.90	74	22(13)
7	17b	MeCN, Me_4NBF_4[9]	+10	1.1	70	18b(34)
8	17b	DCM-TFA, Bu_4NBF_4[8]	+10	0.90	65	23b(45)
9	17b	MeCN, HBF_4[6]	-35	0.85	92	18b(71); 20b(3); 21b(>0)
10	17b	MeCN, $LiBF_4$[5]	-35	0.85	100	18b(33); 19b(28); 20b(9); 21b(>0)
11	17c	MeCN, HBF_4[6]	-35	1.35	79	18c(26) 24a(49); 26(9M) 27(70); 28
12	17c	MeCN, $LiBF_4$[5]	-35	1.00	76	24a(34); 26(>0)
13	17c	MeCN, HBF_4[6]	-35	0.80	79	18c(16); 24a(64); 26(18)
14	17c	MeCN, H_2O, $LiBF_4$[9]	-35	0.90	67	18c(13) 24a(28); 26(6)
15	17d	MeCN, HBF_4[6]	-35	1.00	66	18d(56) 24b(26); 26(18)
16	17d	MeCN, $LiBF_4$[5]	-35	1.00	80	24b(49): 26(14)
17	17d	MeCN, H_2O, $LiBF_4$[9]	-35	1.00	75	18d(35); 24b(33); 26(13)
18	17e	MeCN, HBF_4[6]	-35	0.85	100	19c(79)

Entry	Compound	Electrolyte	Temp	E(V)[2]	C(%)[3]	Products, yield(%)[4]
19	17e	DCM-TFA, Bu_4NBF_4[8]	-22	1.00	100	23e(69)
20	17e	MeCN, $LiBF_4$[5]	+10	0.85	100	19c(72)

Notes: (*1*) The electrolyses were carried out under nitrogen in a one-compartment cell at controlled potential with platinum as anode. In all experiments 1.5 millimol of the substrate was dissolved in 60 ml of electrolyte. The amount of current, Q, passed through the cell was 3 Faradays (F) per mol in experiment 6. In all other experiments Q = 2 F/mol.* (*2*) The anode potential, E, was measured relative to a saturated calomel electrode (SCE) in experiments 5 and 7. In all the other experiments the reference was Ag/Ag^+. The SCE potential can be converted to the (Ag/Ag^+)-potential by subtraction of 0. V. (*3*) The conversion, C, is calculated from the amount of unchanged starting material isolated after work-up. (*4*) The yields are based on converted starting material. The usual chemical yield based on total amount of starting material is obtained by multiplication of the yield with the conversion. (*5*) 0.5 g of $LiBF_4$ in 60 ml of Acetonitrile (MeCN). (*6*) 2 ml of 35% aqueous HBF_4 in 60 ml of MeCN. (*7*) 0.5 ml of conc. H_2SO_4 and 1.5 ml H_2O in 60 ml of MeCN. (*8*) 60 ml of 5:1 dichloromethane (DCM); trifluoroacetic acid (TFA) and 0.5 g of nBu_4NBF_4. (*9*) 2 ml of H_2O and 0.5 g of $LiBF_4$ in 60 ml of MeCN.

* At first the electrolyses of 17a were carried out at 10°C. However, at this temperature the conversion after 2F/mol was very low and no product could be isolated.

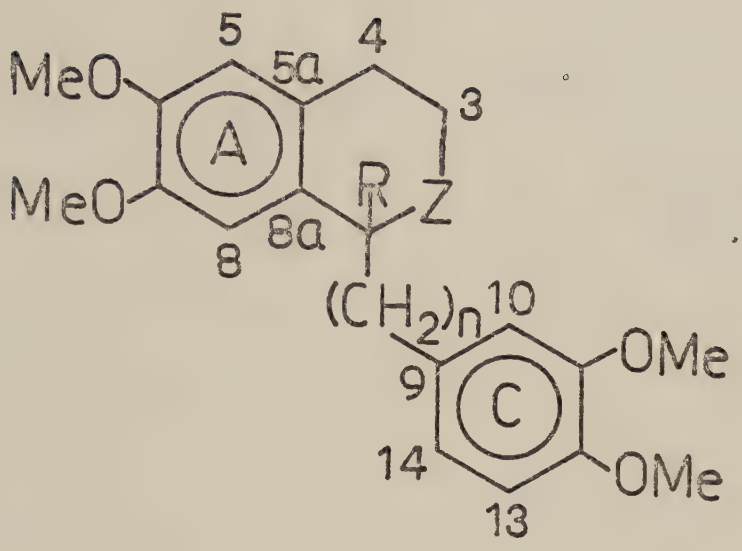
Table 2

Voltammetric data for the oxidation of compounds 17a and 17c-d and the products obtained on electrolysis of these compounds*.

Substrate/electrolysis products	E_{rev} (Volts)†
17a	0.800; 0.930; 1.050; 1.185
18a	0.955
19a	0.970
21a	0.795; 0.920
22	0.595
25	0.855
17e	0.790; 1.065
19c	0.905
23c	0.855

Substrate/electrolysis products	Elev (Volts)†
17c	0.915; 1.200
18c	0.955
24a	0.90 (irreversible)
17d	0.885; 1.205
18d	1.000

*See Table 1 † Estimated reversible potentials from second harmonic measurements relative to an Ag/Ag^+-acetonitrile reference electrode in acetonitrile containing nBu_4NBF_4 (0.2 M). These values can be converted to the saturated calomel reference scale by adding 0.345 V.



17

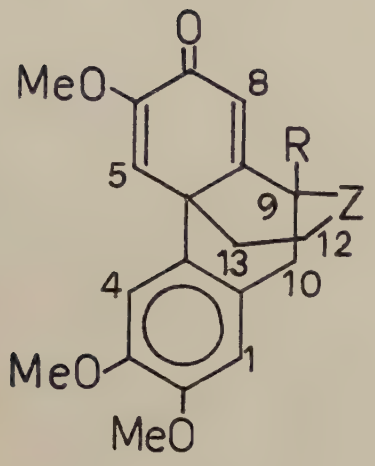
a: Z = CH_2; R = H; n = 1

b: Z = CH_2; R = Me; n = 1

c: Z = O; R = H; n = 1

d: Z = O; R = Me; n = 1

e: Z = CH_2; R = H; n = 2



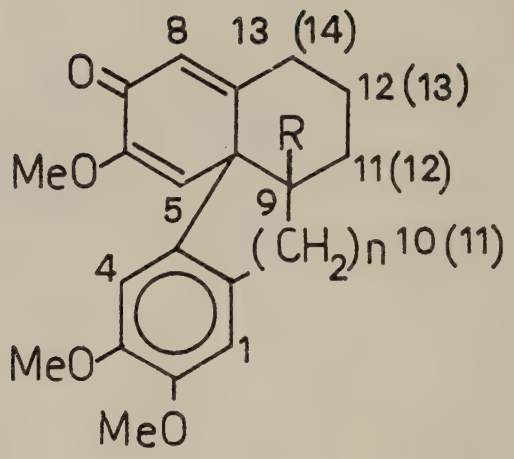
18

a: Z = CH_2; R = H

b: Z = CH_2; R = Me

c: Z = O; R = H

d: Z = O; R = Me

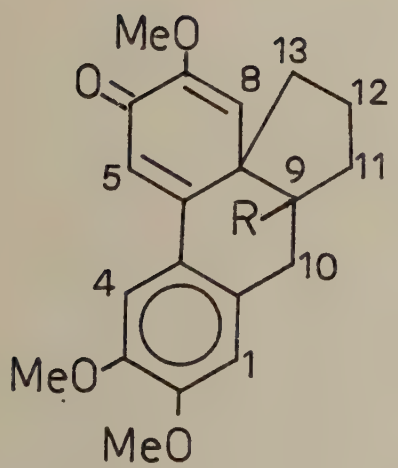


19

a: R = H; n = 1

b: R = Me; n = 1

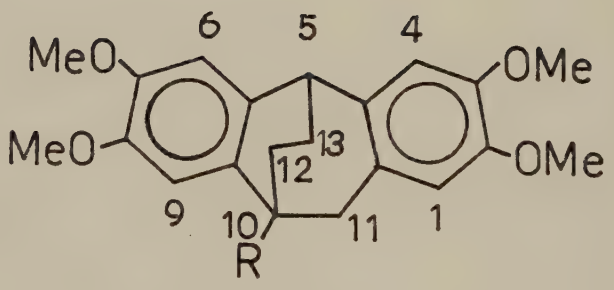
c: R = H; n = 2



20

a: R = H

b: R = Me



21

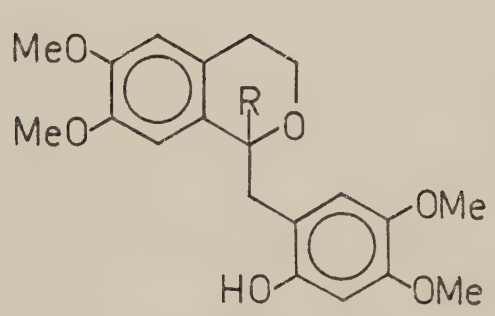
a: R = H

b: R = Me

23 a: R = H; n = 1

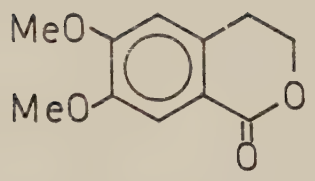
b: R = Me; n = 1

c: R = H; n = 2

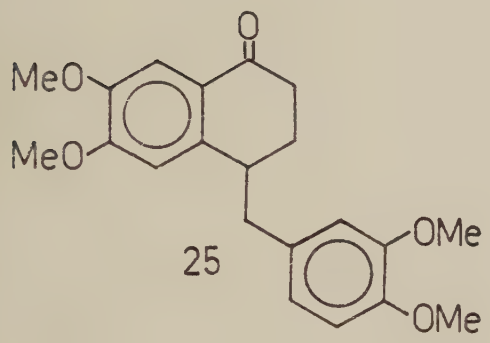


24 a: R = H

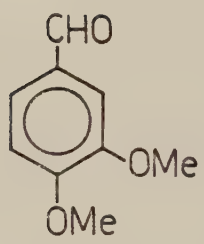
b: R = Me



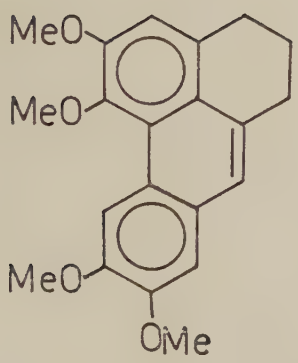
26



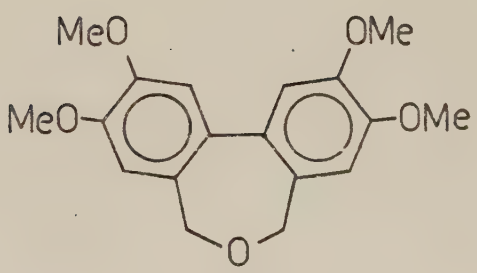
25



27



22



28

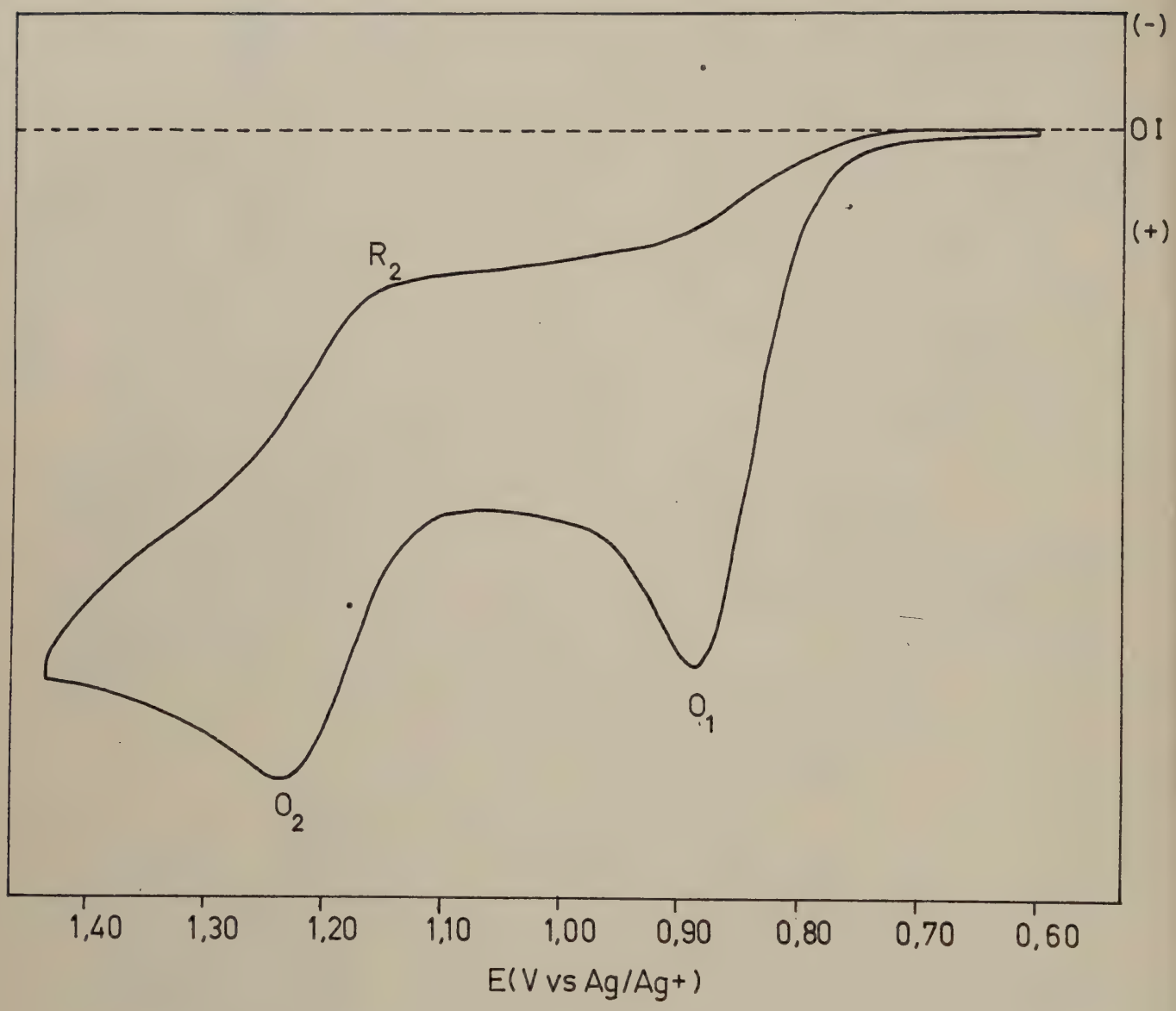
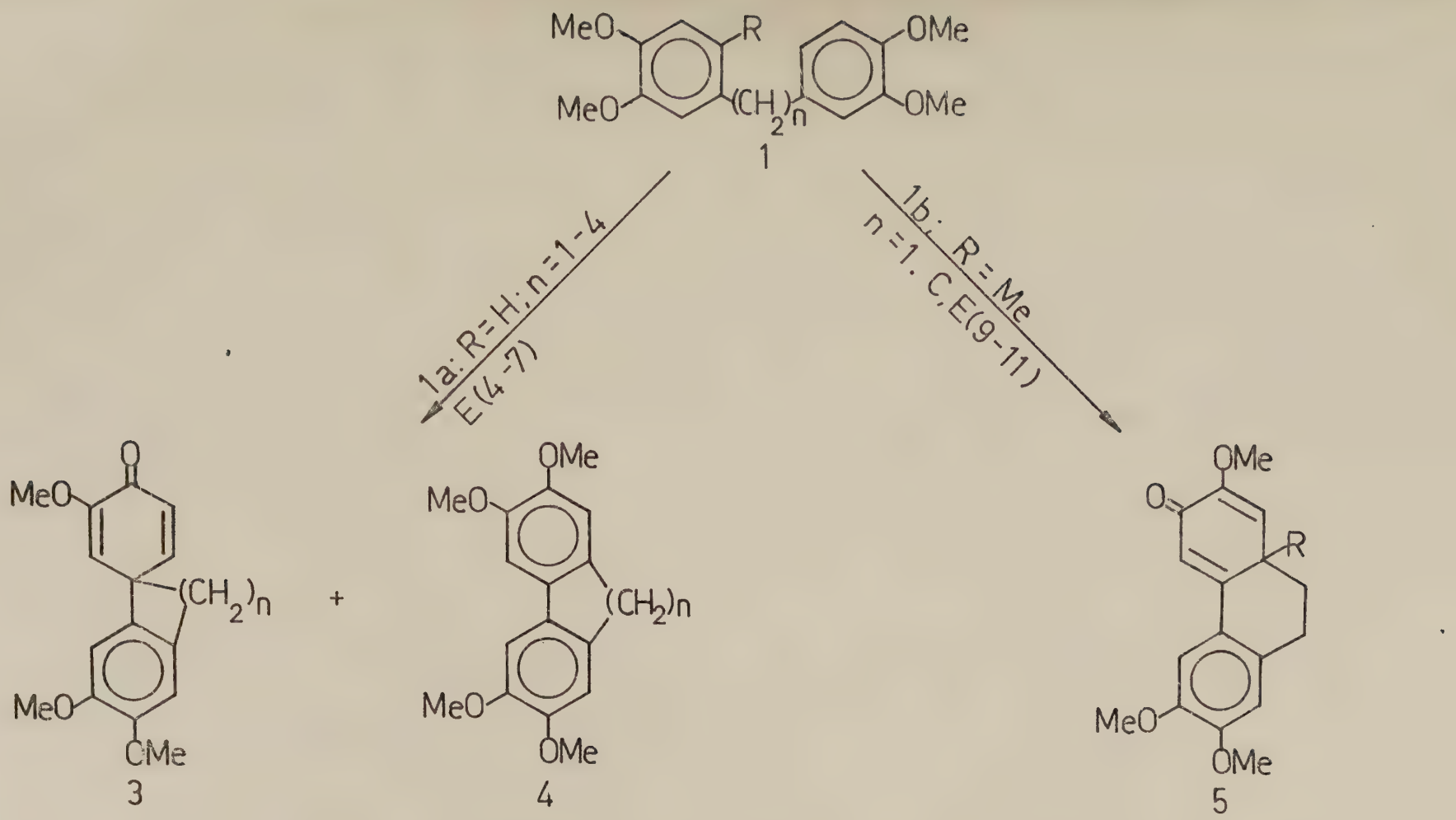
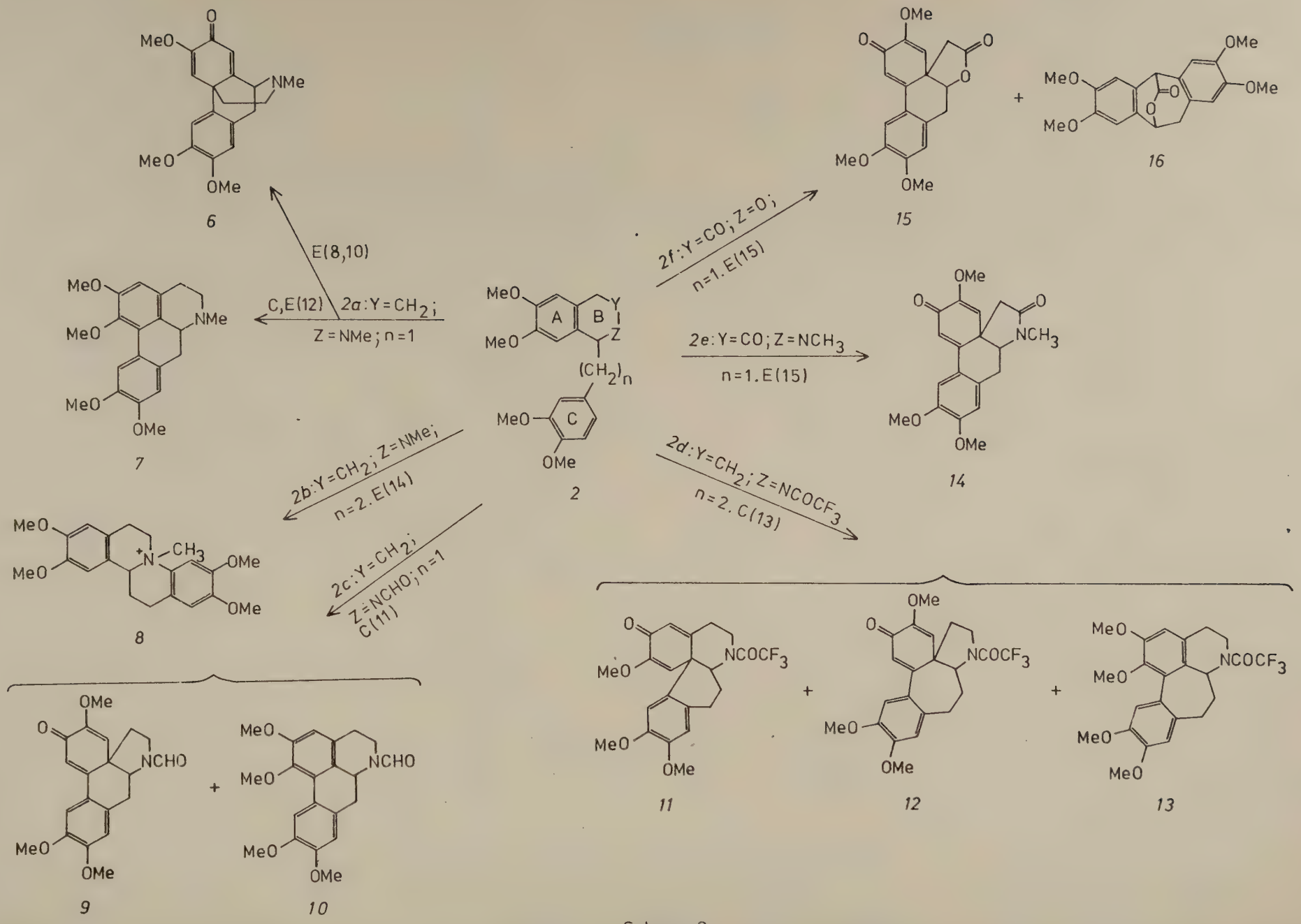


Figure1

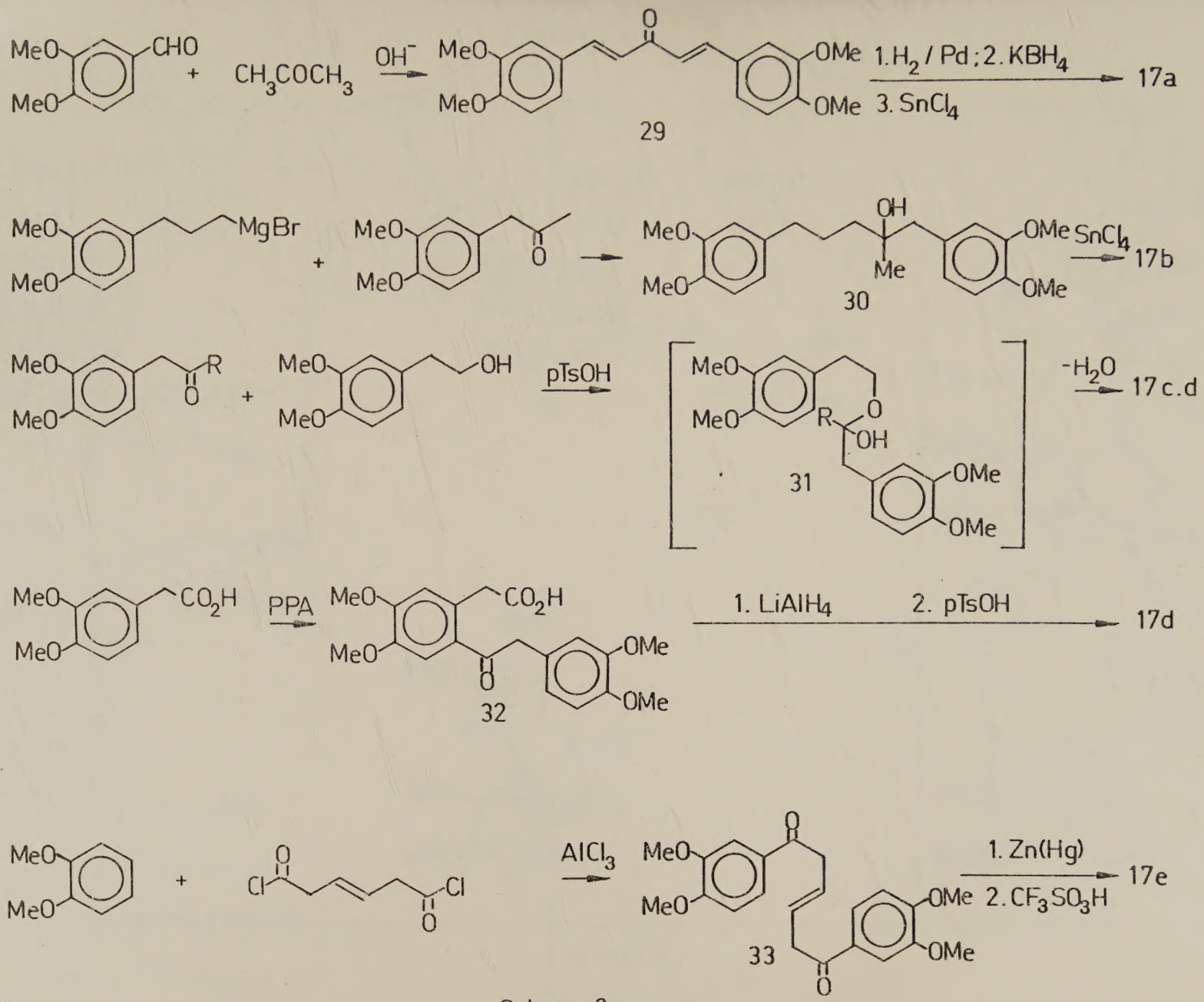


C refers to chemical oxidation with VOF_3 in TFA. E refers to electrochemical oxidation
The numbers in brackets are lit.refs.

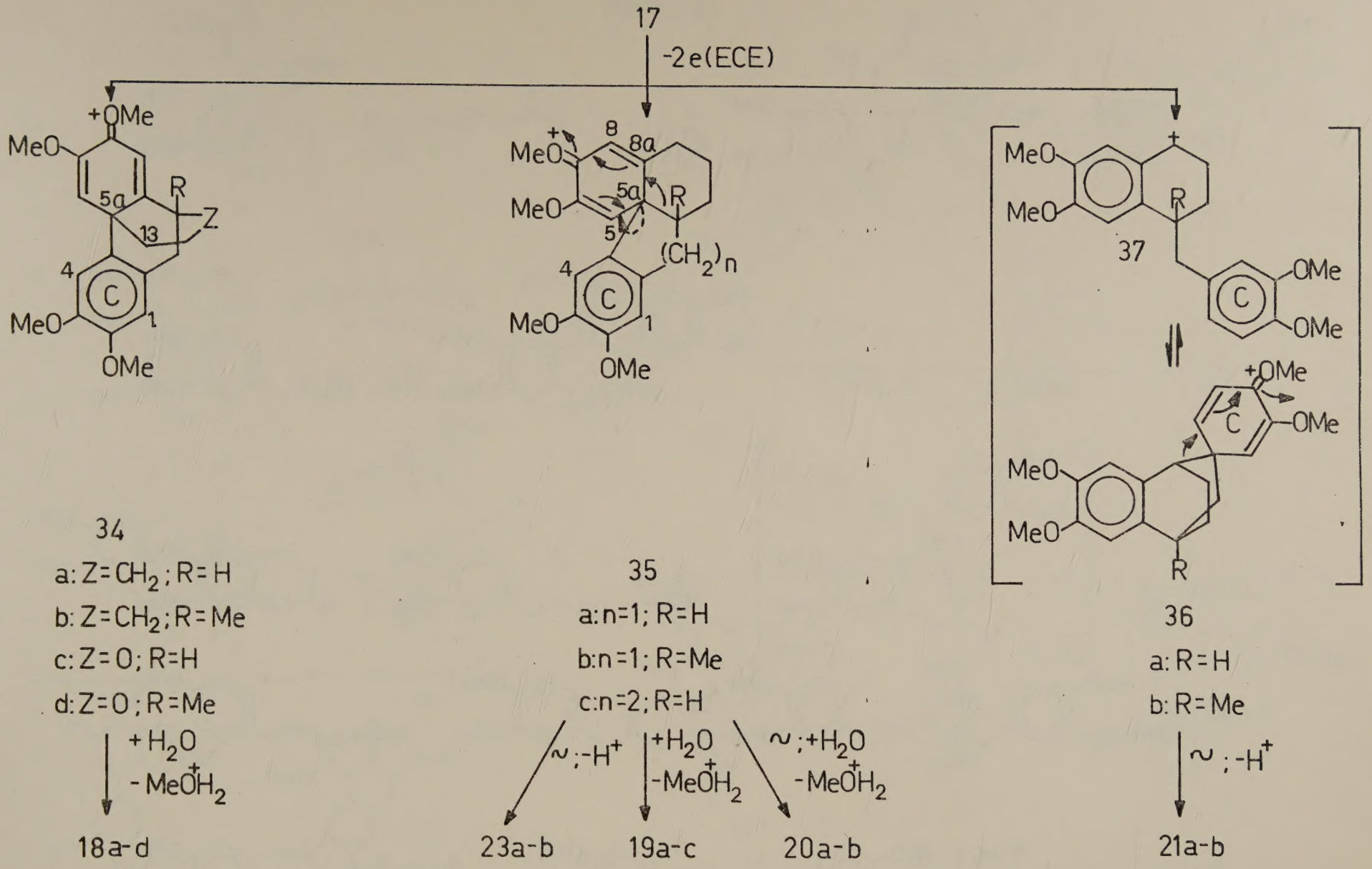
Scheme 1


6
E(8,10)
C,E(12)
2a: Y = CH2; Z = NMe; n = 1
7
2b: Y = CH2; Z = NMe; n = 2. E(14)
8
2c: Y = CH2; Z = NCHO; n = 1 C(11)
9
10
2
2f: Y = CO; Z = O; n = 1. E(15)
15
16
2e: Y = CO; Z = NCH3 n = 1. E(15)
14
2d: Y = CH2; Z = NCOCF3 n = 2. C(13)
11
12
13

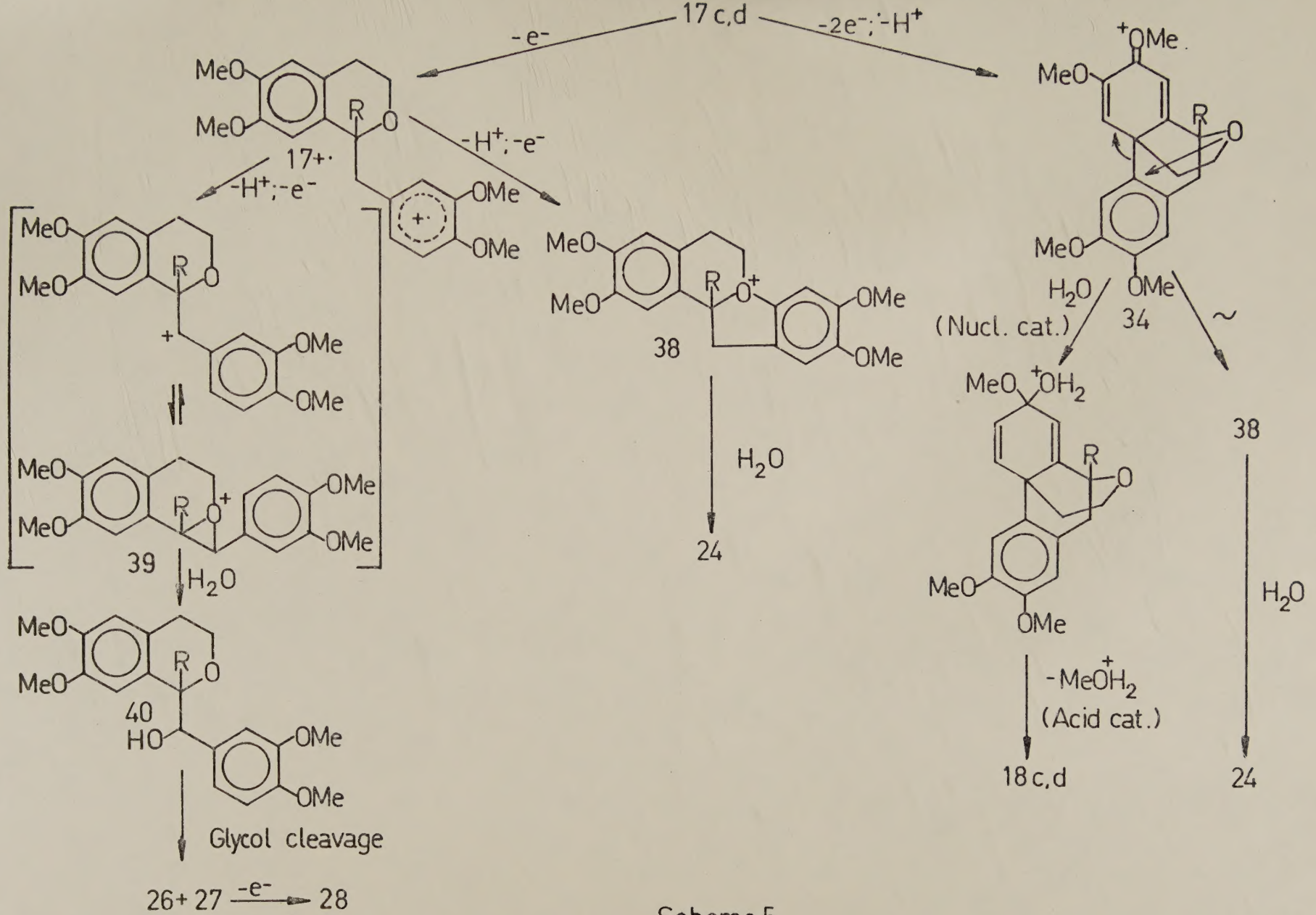
Scheme 2


MeO
MeO
CHO
+
CH_3COCH_3
OH^-
OMe
OMe
29
1. H_2 / Pd ; 2. KBH_4
3. $SnCl_4$
17a
MgBr
OH
Me
30
$SnCl_4$
17b
R
OH
pTsOH
$-H_2O$
17 c.d
31
CO_2H
PPA
32
1. $LiAlH_4$
2. pTsOH
17d
Cl
$AlCl_3$
33
1. Zn(Hg)
2. CF_3SO_3H
17e

Scheme 3


17
-2e(ECE)
+OMe
MeO
5a
R
Z
13
4
C
1
MeO
OMe
34
a: Z=CH2; R=H
b: Z=CH2; R=Me
c: Z=O; R=H
d: Z=O; R=Me
+H2O
-MeOH2+
18a-d
8
8a
5a
R
5
(CH2)n
4
C
1
MeO
MeO
OMe
35
a: n=1; R=H
b: n=1; R=Me
c: n=2; R=H
~; -H+
+H2O
-MeOH2+
~; +H2O
-MeOH2+
23a-b
19a-c
20a-b
MeO
MeO
R
37
OMe
OMe
C
+OMe
OMe
MeO
MeO
R
36
a: R=H
b: R=Me
~; -H+
21a-b

Scheme 4


17 c,d
-e⁻
-2e⁻;-H⁺
17+·
-H⁺;-e⁻
-H⁺;-e⁻
MeO
MeO
R
O
OMe
OMe
38
39
40
HO
H₂O
24
(Nucl. cat.)
34
-MeOH₂
(Acid cat.)
18 c,d
Glycol cleavage
26+27 -e⁻ 28

Scheme 5

Legend to Figure 1 and Schemes:

Figure 1: Cyclic voltammogram for the oxidation of 17d in acetonitrile containing nBu_4NBF_4 (0.2 M). Voltage sweep rate 50 mVs^{-1}. Ag/Ag^+ reference electrode.

Scheme 1. C refers to a chemical oxidation with vanadium oxyfluoride. E refers to an electrochemical oxidation. The numbers in brackets are literature references.

Scheme 2. C refers to a chemical oxidation with vanadium oxyfluoride in TFA. E refers to an electrochemical oxidation. The numbers in brackets are literature references.

Scheme 3. Syntheses of compounds 17a-e. For details see Experimental

Scheme 4. Possible mechanisms for the formation of compounds 18a-d, 19a-c, 20a-b, 21a-b, and 23a-b. ~ Signifies a rearrangement reaction. -e indicates loss of one electron.

Scheme 5. Possible mechanisms for the anodic formation of compounds 18c-d, 24, 27 and 27. ~ signifies a rearrangement . -e indicates loss of one electron.